

**UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS**

ASTELLAS INSTITUTE FOR REGENERATIVE
MEDICINE, and STEM CELL & REGENERATIVE
MEDICINE INTERNATIONAL, INC.,

Plaintiffs,

v.

IMSTEM BIOTECHNOLOGY, INC., XIAOFANG
WANG, and REN-HE XU,

Defendants.

C.A. No. 1:17-cv-12239

DEFENDANT REN-HE XU'S ANSWER

Defendant Dr. Ren-He Xu ("Dr. Xu") hereby Answers the Complaint of Plaintiffs Astellas Institute for Regenerative Medicine ("Astellas") and Stem Cell & Regenerative Medicine International, Inc. ("SCRMI") (collectively "Plaintiffs") as follows:

INTRODUCTION

1. Defendant admits that this action concerns the creation of mesenchymal stem cells and that the mesenchymal stem cells are useful in treating various disorders, including multiple sclerosis. Defendant denies the remaining allegations contained in Paragraph 1.

2. Defendant admits that Astellas and SCRMI focus on research regarding regenerative medicine. Defendant further admits that Dr. Lu and Dr. Lanza published an article in Nature Methods in 2007 on a method for generating hemangioblasts from embryonic stem cells. Defendant admits that hemangioblasts are a specialized type of progenitor cell derived from human embryonic stem cells that are useful in the field of regenerative medicine because they can be differentiated into a number of different cell types used for the treatment of various

diseases. Defendant lacks knowledge or information sufficient to admit or deny the remaining allegations contained in Paragraph 2.

3. Defendant admits that Dr. Kimbrel and Dr. Lanza developed a method for differentiating embryonic stem cells into mesenchymal stem cells via a hemangioblast intermediate. Defendant denies that Dr. Kimbrel and Dr. Lanza thought of the idea of using the mesenchymal stem cells they created to treat autoimmune diseases like multiple sclerosis. Defendant lacks knowledge or information sufficient to admit or deny the remaining allegations contained in Paragraph 3.

4. Defendant denies that SCRMI was a small company at the time. Upon information and belief, SCRMI was a subsidiary of a publicly traded company. Defendant admits the remaining allegations contained in Paragraph 4.

5. Defendant denies that Dr. Lu knew that Defendant had access to the EAE mouse model. Defendant admits that Dr. Lu introduced Dr. Wang to Dr. Kimbrel to discuss a potential collaboration in response to an inquiry from Dr. Wang. Defendant admits that Dr. Kimbrel and Dr. Wang corresponded. Defendant admits that plaintiffs possessed certain technology related to generating mesenchymal stem cells and that they shared such information with him and Dr. Wang for purposes of the collaboration. Defendant admits that he submitted a grant application in January 2011 for further studies on the use of MSCs in the EAE model. Defendant lacks knowledge or information sufficient to admit or deny the remaining allegations contained in Paragraph 5.

6. Defendant admits that the test results from the EAE mouse experiments were positive and that he, Dr. Kimbrel, and Dr. Wang worked together on an article that was published in Stem Cell Reports in July 2014. Defendant denies the remaining allegations contained in

Paragraph 6.

7. Defendant admits that he and Dr. Wang formed ImStem in or about June 2012 and filed Application No. 14/413,290 with the United States Patent and Trademark Office, which became Patent No. 9,745,551 (the “551 Patent”). Defendant further admits that he and Dr. Wang represented to the PTO that they had invented a method for differentiating mesenchymal stem cells from hemangioblasts using a GSK3 inhibitor and feeder free culture medium. Defendant denies the remaining allegations contained in Paragraph 7.

8. Denied.

NATURE OF THE ACTION

9. Paragraph 9 contains legal conclusions to which no response is required.

THE PARTIES

10. Defendant lacks knowledge or information sufficient to admit or deny the allegations contained in Paragraph 10.

11. Defendant lacks knowledge or information sufficient to admit or deny the allegations contained in Paragraph 11.

12. Admitted.

13. Admitted.

14. Defendant admits that he was the Chief Scientific Officer of ImStem as well as one of ImStem’s founders and is currently employed by the University of Macau. Defendant denies the remaining allegations contained in Paragraph 14.

SUBJECT MATTER JURISDICTION AND VENUE

15. Paragraph 15 contains legal conclusions to which no response is required.

16. Paragraph 16 contains legal conclusions to which no response is required.

17. Paragraph 17 contains legal conclusions to which no response is required.

PERSONAL JURISDICTION

18. Admitted.

19. Admitted.

20. Defendant admits that he and Dr. Wang visited plaintiffs' facility in Marlborough, Massachusetts during their collaboration with Dr. Kimbrel and Dr. Lanza for various reasons, including to collect cells and other materials necessary for their work in the collaboration. Defendant denies the remaining allegations contained in Paragraph 20.

21. Admitted.

22. Admitted.

23. Admitted. Further answering Paragraph 23, Defendant avers that he and Dr. Wang had their own grant funding to conduct the MSC studies and often used their own grant funds to purchase materials in furtherance of the collaboration.

24. Defendant admits that he and Dr. Wang traveled to plaintiffs' Marlborough, Massachusetts facility during their collaboration. Defendant denies the remaining allegations contained in Paragraph 24.

25. Paragraph 25 contains legal conclusions to which no response is required.

26. Paragraph 26 contains legal conclusions to which no response is required.

27. Paragraph 27 contains legal conclusions to which no response is required.

28. Paragraph 28 contains legal conclusions to which no response is required.

FACTUAL BACKGROUND

Plaintiffs' Development of Methods for Generating Mesenchymal Stem Cells

29. Defendant admits that Dr. Kimbrel and Dr. Lanza developed a method for

generating hemangioblasts. Defendant admits that hemangioblasts are a specialized type of progenitor cell derived from human embryonic stem cells that are useful in the field of regenerative medicine because they can be differentiated into a number of different cell types used for the treatment of various diseases. Defendant denies the remaining allegations contained in Paragraph 29.

30. Defendant admits that Dr. Lu and Dr. Lanza, along with others, published an article in Nature Methods in 2007 on a method for generating hemangioblasts from embryonic stem cells. Defendant avers that the article published by the journal Nature Methods speaks for itself and requires no further response.

31. Defendant lacks knowledge or information sufficient to admit or deny the allegations contained in Paragraph 31.

32. Defendant denies that Dr. Kimbrel and Dr. Lanza thought of the idea to use the mesenchymal stem cells they created to treat autoimmune diseases like multiple sclerosis. Defendant lacks knowledge or information sufficient to admit or deny the remaining allegations contained in Paragraph 32.

Plaintiffs' Collaboration with Drs. Xu and Wang

33. Defendant denies that Dr. Kimbrel and Dr. Lanza sought to find collaborators with animal facilities and experience with animal models of autoimmune diseases, including the EAE mouse model. Defendant admits the remaining allegations contained in Paragraph 33.

34. Defendant admits Dr. Lu introduced Dr. Kimbrel to Dr. Wang about a potential collaboration and that Dr. Wang suggested testing the mesenchymal stem cells in the EAE mouse model. Defendant denies that Dr. Lu knew that they had access to the EAE mouse model. Defendant lacks knowledge or information sufficient to admit or deny the remaining allegations

contained in Paragraph 34.

35. Defendant admits that Drs. Wang and Lu visited SCRMI in or about August 2010 and collected frozen MSCs for experiments in furtherance of the parties' collaboration. Defendant further admits that, following the meeting at SCRMI, Dr. Kimbrel shared a protocol for differentiating hemangioblasts into MSCs based largely on the protocol that Dr. Lu and Dr. Lanza had previously published in Nature Methods. Defendant denies the remaining allegations contained in Paragraph 35.

36. Defendant denies that Dr. Kimbrel and Dr. Lanza provided data that demonstrated that the cells generated from their protocol were, in fact, mesenchymal stem cells. Defendant admits the remaining allegations contained in Paragraph 36.

37. Admitted.

38. Defendant lacks knowledge or information sufficient to admit or deny the allegations contained in Paragraph 38.

39. Defendant admits that a Material Transfer Agreement was proposed but never executed. Defendant denies the remaining allegations contained in Paragraph 39.

40. Defendant admits that in the course of the parties' collaboration, and in connection with the work performed by him and Dr. Wang during that collaboration, he and Dr. Wang requested certain supplies from Drs. Kimbrel and Lanza.

41. Admitted.

42. Denied.

43. Defendant admits that he and Dr. Wang continued collaborating with Dr. Kimbrel and Dr. Lanza during 2012 through 2013, including working together to draft an article that was published in Stem Cell Reports. Defendant further admits that discord developed as a result of

Dr. Kimbrel and Dr. Lanza's decision to publish their own paper separately in a lesser-known journal, causing the collaboration's paper to be rejected from the journal to which it was submitted for publication Cell Stem Cell. Defendant denies all remaining allegations contained in Paragraph 43.

44. Admitted.

45. Admitted.

Dr. Xu and Dr. Wang Form ImStem and File Patent Application

46. Defendant admits that in or about June 2012, he and Dr. Wang formed ImStem Biotechnology, Inc. and were awarded funding and lab space for stem cell research. Defendant denies the remaining allegations contained in Paragraph 46.

47. Defendant admits that in or about July 2012 and February 2013, he and Dr. Wang filed the provisional applications that led to the '551 Patent. The '551 Patent claims a method for differentiating hESCs into MSCs using a GSK3 inhibitor and feeder free culture medium. Dr. Wang's method is materially different from the protocol that Dr. Kimbrel shared with Dr. Wang for purposes of their collaboration. Dr. Wang developed his method through his own efforts, separate and apart from the work of the collaboration. Dr. Wang further never disclosed the GSK3 inhibitor method to Dr. Kimbrel or anyone else. Defendant denies the remaining allegations contained in Paragraph 47.

48. Defendant admits that he knew Dr. Kimbrel and Dr. Lanza had filed a patent application on their protocol for differentiating hemangioblasts into MSCs. Defendant further admits that he and Dr. Wang signed a declaration dated January 12, 2017, stating that they possessed the subject matter of the '551 Patent before November 30, 2011. Further answering Paragraph 48, Defendant states that he believed Dr. Kimbrel and Dr. Lanza's protocol for

differentiating MSCs contained only obvious, public information. Defendant therefore did not believe that Dr. Kimbrel and Dr. Lanza had contributed anything significant to Dr. Wang's method of differentiating MSCs using a GSK3 inhibitor and feeder free culture medium.

49. Admitted.

50. Defendant admits that Plaintiffs possessed certain technology related to generating mesenchymal stem cells and that they shared such information with Defendant for purposes of the collaboration. Defendant denies that the '551 Patent claims Plaintiffs' technology. Dr. Wang developed the method claimed in the '551 through his own efforts, separate and apart from the work of the collaboration. Defendant denies the remaining allegations contained in Paragraph 50.

COUNT I

(Correction of Inventorship for the '551 Patent: Drs. Kimbrel and Lanza as Sole Joint Inventors)

51. Defendant's answers to Paragraphs 1-50 are incorporated herein by reference.

52. Denied.

53. Denied.

54. Denied.

COUNT II

(In the Alternative, Correction of Inventorship for the '551 Patent: Drs. Kimbrel and Lanza as Joint Inventors with the Currently Named Inventors)

55. Defendant's answers to Paragraphs 1-54 are incorporated herein by reference.

56. Denied.

57. Defendant lacks knowledge or information sufficient to admit or deny the allegations in Paragraph 57.

58. Denied.

COUNT III
(Conversion)

59. Defendant's answers to Paragraphs 1-58 are incorporated herein by reference.

60. Defendant admits that Plaintiffs possessed certain technology related to generating mesenchymal stem cells and that they shared such information with him and Dr. Wang for purposes of the collaboration. Defendant denies that Plaintiffs initially shared this information under strict restrictions regarding its use. Defendant denies the remaining allegations contained in Paragraph 60.

61. Denied.

62. Denied.

63. Denied.

COUNT IV
(Unjust Enrichment)

64. Defendant's answers to Paragraphs 1-63 are incorporated herein by reference.

65. Denied.

66. Denied.

67. Denied.

68. Denied.

69. Denied.

70. Denied.

COUNT V
(Unfair Trade Practices Under Massachusetts General Law Chapter 93A)

71. Defendant's answers to Paragraphs 1-70 are incorporated herein by reference.

72. Paragraph 72 contains legal conclusions to which no response is required.

73. Denied.

74. Denied.

75. Denied.

76. Denied.

COUNT VI
(Misappropriation of Trade Secrets)

77. Defendant's answers to Paragraphs 1-76 are incorporated herein by reference.

78. Defendant admits that he and Dr. Wang received certain scientific information relating to the generation of MSCs during the course of the parties' collaboration. Defendant denies the remaining allegations contained in Paragraph 78.

79. Defendant admits that sometime after the parties' collaboration had commenced Dr. Kimbrel sought assurances that any new information shared by Plaintiffs going forward would be treated confidentially for the purposes of further collaboration between the parties. Defendant denies the remaining allegations contained in Paragraph 79.

80. Denied.

81. Denied.

COUNT VII
(Negligent Misrepresentation)

82. Defendant's answers to Paragraphs 1-81 are incorporated herein by reference.

83. Defendant admits that sometime after the parties' collaboration had commenced Dr. Kimbrel sought assurances that any new information shared by Plaintiffs going forward would be treated confidentially for the purposes of further collaboration between the parties. Defendant further admits that on or about January 12, 2017, he and Dr. Wang filed a declaration with the United States Patent and Trademark Office declaring that they are the original inventors of the subject matter of the '551 Patent. Defendant denies the remaining allegations contained in

Paragraph 83.

84. Denied.

JURY DEMAND

85. Paragraph 85 does not require a response.

PRAYER FOR RELIEF

86. Defendant denies that Plaintiffs are entitled to the relief requested in the Complaint. To the extent that any statement in the Prayer for Relief is deemed factual, it is denied.

AFFIRMATIVE DEFENSES

Further answering the Complaint, Defendant asserts the following defenses, without assuming the burden of proof where such burden would otherwise be on the Plaintiff. Defendant reserves the right to assert additional defenses as further information is obtained.

**FIRST AFFIRMATIVE DEFENSE
(Failure to State a Claim)**

The Complaint fails to state a claim upon which relief may be granted.

**SECOND AFFIRMATIVE DEFENSE
(Laches)**

Plaintiffs' claims are barred, in whole or in part, by the doctrine of laches.

**THIRD AFFIRMATIVE DEFENSE
(Unclean Hands)**

Plaintiffs' claims are barred, in whole or in part, by the doctrine of unclean hands.

June 8, 2018

Respectfully submitted,

DEFENDANT DR. REN-HE XU

By his attorneys,

/s/ Timothy R. Shannon

Timothy R. Shannon, MA Bar # 655325

VERRILL DANA LLP

One Portland Square

P.O. Box 586

Portland, Maine 04112-0586

(207) 774-4000

tshannon@verrilldana.com

CERTIFICATE OF SERVICE

I hereby certify that on June 8, 2018, I caused a true copy of the foregoing document to be served upon all counsel of record via the Court's CM/ECF electronic filing system.

/s/ Timothy R. Shannon

Timothy R. Shannon